

REMARKS

Amendments in the claims

Following entry of the present amendment, Claims 12–28 are pending in the present application, of which Claims 20–28 are presently withdrawn from consideration.

Claim 12 is amended to replace the term “dispergents” with “dispersants”. Applicant believes that one of skill in the art would readily understand from reading the specification as a whole that the term “dispergent” equates to what is more familiarly in English called a “dispersing agent” or “dispersant”. The word “dispergent” is used throughout the present specification; in the German-language priority document, DE 102 61 696, the corresponding word is “Dispersionsmittel” which is translatable as “dispersant”.

Claim 12 is further amended to delete recitation of a matrix polymer “supersaturated” with rotigotine base and insert in its place “rotigotine base in a concentration above the solubility limit of rotigotine base in the matrix polymer,” in alignment with Claim 13. Support is found in the specification as filed, for example at p. 6, line 22 thereof: “(b) rotigotine base in a concentration above the solubility limit of the matrix polymer.” One of skill in the art will understand this to mean “... above the solubility limit of the rotigotine base in the matrix polymer” or “... above the solubility limit of the matrix polymer for the rotigotine base”.

Claim 13 is amended, like Claim 12, to more precisely recite rotigotine base in a concentration above the solubility limit of rotigotine base in the matrix polymer.” Claims 12 and 13 are each amended to insert the word “base” after “rotigotine in the “wherein” clause for clearer antecedent basis.

Claim 19 is amended to correct “mg/cm³” to “mg/cm²”. This was a typographical error, as evidenced by the paragraph bridging pp. 11–12 of the specification as filed, where the units are repeatedly shown as “mg/cm²”. Claim 19 is also amended to recite that “the rotigotine is present in amount of 0.3 to 6 ...” in place of the recitation “the rotigotine charge is between 0.3 to 6 ...”, which as previously rendered could have been found to lack literal antecedent basis for “the rotigotine charge” and to be unclear as to whether the amount present was “0.3 to 6” mg/cm² or “between 0.3 and 6” mg/cm². The above-referenced paragraph bridging pp. 11–12 of the specification as filed clarifies that “0.3 to 6” mg/cm² was intended.

No new matter is introduced as a result of the present amendment.

RESPONSE TO OFFICE ACTION DATED AUGUST 6, 2008

1. Priority

In the present Action, the Examiner acknowledges Applicant's submission under 35 U.S.C. §119(a)–(d) and states that no English-language translation of the foreign priority application has been received. Applicant does not believe that a translation is required at this time. Under 37 C.F.R. 1.55(a)(4), an English-language translation of a non-English-language foreign application is not required except under certain circumstances. Applicant does not believe that any of the recited circumstances apply in this case.

At the present time, to the knowledge of the undersigned, no English-language translation of the priority application has been prepared. Should such a translation be required for any reason, the Examiner is requested to call the undersigned at the number below.

2. Claim objections

Claims 12 and 13 [*sic*; 19 believed intended] are objected to as having typographical errors. Following amendment of Claims 12 and 19 herein, these objections are moot and withdrawal of the present objections is respectfully requested.

3. Rejection under 35 U.S.C. §103(a)

Claims 12–19 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over U.S. Patent Application Publication No. 2003/0027793 (“Lauterbach”) in view of U.S. Patent No. 5,906,830 (“Farinas”) and International Patent Publication No. WO 92/014442 (“Taylor”). This rejection is respectfully traversed.

At the outset it is noted that the publication date of Lauterbach (February 6, 2003), is later than the earliest priority date of the present application (December 30, 2002). The Examiner's attention is respectfully drawn to International Patent Publication No. WO 02/089777, published November 14, 2002, which appears to be a counterpart of the Lauterbach reference. Lauterbach does not constitute statutory prior art under 35 U.S.C. §102(b), and no admission is made herein that the disclosure of Lauterbach constitutes prior art to the present invention under any section of 35 U.S.C. §102. Applicant reserves the right to make a showing of earlier invention to disqualify Lauterbach. However, such a showing is unnecessary, as even if Lauterbach represented prior art to the present invention, Lauterbach

would not render the present claims obvious, for reasons set forth below.

The present Action asserts that one of skill would have been motivated to use a matrix free of solvents, crystallization inhibitors and dispersants to reduce cost, time and effort. However, even if such motivation existed (which is not admitted herein), that is not enough to establish a *prima facie* case of obviousness.

Reasonable expectation of success has long been a required criterion for a *prima facie* case of obviousness. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). In recently redefining the standards for determining obviousness, the U.S. Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 82 USPQ2d 1385 (2007), has confirmed that “[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results” (emphasis added). See also MPEP 2143.01.III: “The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art” (emphasis in original).

With respect to Claim 12, it could not have been predicted by one of skill in the art at the time of the present invention that a storage-stable matrix could be prepared containing rotigotine base above its limit of solubility in the matrix polymer, yet without solvents, crystallization inhibitors or dispersants. With respect to Claim 13, it could not have been predicted by one of skill in the art at the time of the present invention that a storage-stable matrix could be prepared containing rotigotine base above its limit of solubility in the matrix polymer, yet without any excipient ingredient other than the matrix polymer and, optionally, one or more antioxidants. Thus, the present rejection is traversed on the ground that no reasonable expectation of success existed at the time of the present invention, or, per *KSR v. Teleflex*, that the results would not have been predictable to one of ordinary skill in the art.

In describing the differences between Lauterbach and the present claims, the Examiner states that Lauterbach *et al.* “do not teach a transdermal system comprising a matrix polymer supersaturated with rotigotine base” (Action, p. 6, lines 18–19). Applicant notes for the record that the term “supersaturated” as defined in the present application does not necessarily imply supersaturation in the classical sense of a solution in which a solute is dissolved at a concentration above its normal limit of solubility. See specification as filed at p. 8, lines 1–3:

In this patent application the expression “matrix supersaturated with rotigotine” is understood to mean that at least a portion of the rotigotine is not in the form dissolved in the polymer but rather dispersed as particles in the matrix.

There is thus no requirement in the present claims for the matrix to contain dissolved rotigotine base above its normal limit of solubility in the matrix (a point clarified by amendment of Claim 12 herein), and “supersaturation” is therefore not a point of distinction of the instant claims over Lauterbach. Rather, a significant distinction between the instant claims and the Lauterbach art lies in the fact that the matrix of the present invention is free of solvents, crystallization inhibitors and dispersants.

Specifically, as discussed in the present specification as filed at p. 2, lines 18–20: “Rotigotine is only feebly soluble in hydrophobic polymers such as silicon[e], for example. For these reasons, in WO 99/49852 the adding of additives to improve the solution characteristics of the rotigotine is recommended.” Lauterbach also references WO 99/49852, for example at paragraphs [0011]–[0013] thereof, and in the preparation example thereof includes such an additive, namely polyvinylpyrrolidone (PVP), together with rotigotine base in a silicone matrix (Lauterbach, paragraphs [0037]–[0041]). Therefore the art of record emphasizes the importance of using a solubility-enhancing ingredient such as PVP in providing a silicone polymer/rotigotine base matrix providing acceptable skin flux of rotigotine.

Against the background of Lauterbach and WO 99/49852 cited therein, the listing by Farinas of crystallization inhibitors or dispersants as “optional” is given excessive weight by the present Action at p. 7, lines 8–11. It is essential to note that while Lauterbach, the primary reference, addresses a solubility issue when using rotigotine base, the particular drug of interest in the present application, Farinas exemplifies an unrelated compound, namely estradiol, as the active agent in a transdermal composition. Applicant submits that one of skill in the art, if reading Farinas’s disclosure of “optional” inclusion of crystallization inhibitors in combination with Lauterbach, would be led to believe that in the specific case of rotigotine, a crystallization inhibitor would be a necessary ingredient. No rationale has been suggested for one of skill in the art to have gone against the teaching of Lauterbach and WO 99/49852 to attempt to prepare a matrix comprising a matrix polymer and rotigotine base above the limit

of its solubility therein, yet without solvents, crystallization inhibitors or dispersants.

The Examiner further cites Taylor as discussing an active agent present in fine particles. However, the present claims are specific in reciting amorphous particles. By contrast, throughout Taylor, various references are made to “crystals” (*i.e.*, particles that are not amorphous), and no reference is found to amorphous particles. For example, Taylor refers to “crystals of biologically active agent ... predominantly sized less than 20 μm ” (Taylor, p. 9, lines 24–25), and, in Example 1, to the particle size of the “ibuprofen crystallites precipitated” (Taylor, p. 12, lines 12–15). Therefore Taylor, read as a whole, does not provide motivation for one of skill in the art to prepare a matrix containing amorphous rotigotine particles.

Additionally, the Examiner cites Taylor as discussing an active agent present in fine particles throughout a carrier wherein at least 60% of the particles are sized at less than 20 μm (although the point is moot, Applicant does not admit that this recitation necessarily equates to a maximum mean diameter of 30 μm , as required by Claims 12 and 13). However, regardless of whether Taylor discusses fine particles of specific size, there is no teaching therein of amorphous particles and, as with Farinas, no motivation therein for one of skill in the art to go against the teaching of Lauterbach and WO 99/49852 to attempt to prepare a matrix comprising a matrix polymer and rotigotine base above the limit of its solubility therein, yet without solvents, crystallization inhibitors or dispersants.

Finally, even if *arguendo* one of ordinary skill would somehow have been motivated to remove the crystallization inhibitors taught in Lauterbach and WO 99/49852 and prepare a matrix comprising rotigotine free base amorphous particles with a maximum mean diameter of 30 μm , it could not have been predicted (as required for a showing of obviousness under the *KSR v. Teleflex* standard) that after 12 months storage, no signs of rotigotine crystallization or change in particle size would be observed, as disclosed in the present specification as filed at p. 6, lines 4–5. Therefore, Applicant submits that no *prima facie* case of obviousness has been established, at least for the reason that the cited art leads neither to predictability of outcome nor to reasonable expectation of success in preparing a storage-stable polymer matrix containing amorphous particles of rotigotine free base.

The Office has thus failed to make a case of *prima facie* obviousness with respect to

Claims 12 or 13. Claims 14–19 each depend directly or ultimately from Claims 12 or 13 and incorporate all limitations of these claims, and are therefore nonobvious for at least the same reasons that Claims 12 and 13 are nonobvious. Withdrawal of the present rejection is respectfully requested.

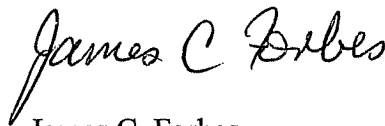
4. Conclusion

It is believed that all of the stated grounds of rejection are properly traversed, accommodated or rendered moot herein. Applicant therefore respectfully requests that the Examiner consider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the present Action and that the application is in condition for allowance.

Should any issues remain, the Examiner is invited to call the undersigned at the telephone number given below.

Respectfully submitted,

HARNESS, DICKEY & PIERCE, P.L.C.

A handwritten signature in cursive script that reads "James C. Forbes".

James C. Forbes
Agent for Applicant
Reg. No. 39,457
Tel. 847-412-6350